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Pyoderma Gangrenosum Associated with Acute Respiratory Distress Syndrome

To the Editor:

Pyoderma gangrenosum is a rare neutrophilic dermatologic disorder that presents as painful necrotic ulcers. It can also involve the lungs and the kidneys. The etiology remains unclear. However, it has recently been reported that cytokines may play a key role in pyoderma gangrenosum's pathogenesis.[1] Similarly, acute respiratory distress syndrome is characterized as lethal acute inflammation within the lung, leading to severe gas exchange abnormalities triggered by active neutrophils and inflammatory cytokines.[2] Here we report the first case of pyoderma gangrenosum associated with acute respiratory distress syndrome.

A 60-year-old man suffering from recurring leg ulcers for 2 years was admitted to our hospital for diagnosis and treatment. Physical examination revealed violaceous necrotic ulcers with painful swelling and erythema on the left lower leg (**Figure A**). A skin biopsy specimen from an ulcer showed inflammatory cell infiltrates including neutrophils in the dermis. Vasculitis was not observed. Vascular ultrasonography found no thrombus or other vascular abnormalities. Blood tests showed prominent elevation of neutrophilic leukocytes and C-reactive protein (white blood cells: 29.7 × 10^3/μL; normal range: 3.5-9.3 × 10^3/μL; neutrophils: 89.6%; normal range: 40-60%; C-reactive protein 18.96 mg/dL; normal range: 0.0-0.3 mg /dL). Ulcers' bacterial cultures were positive for methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Systemic antibiotics were used to control the local infection. However, the ulcers did not respond to antibiotics, and oxygen saturation dropped suddenly to 70% at

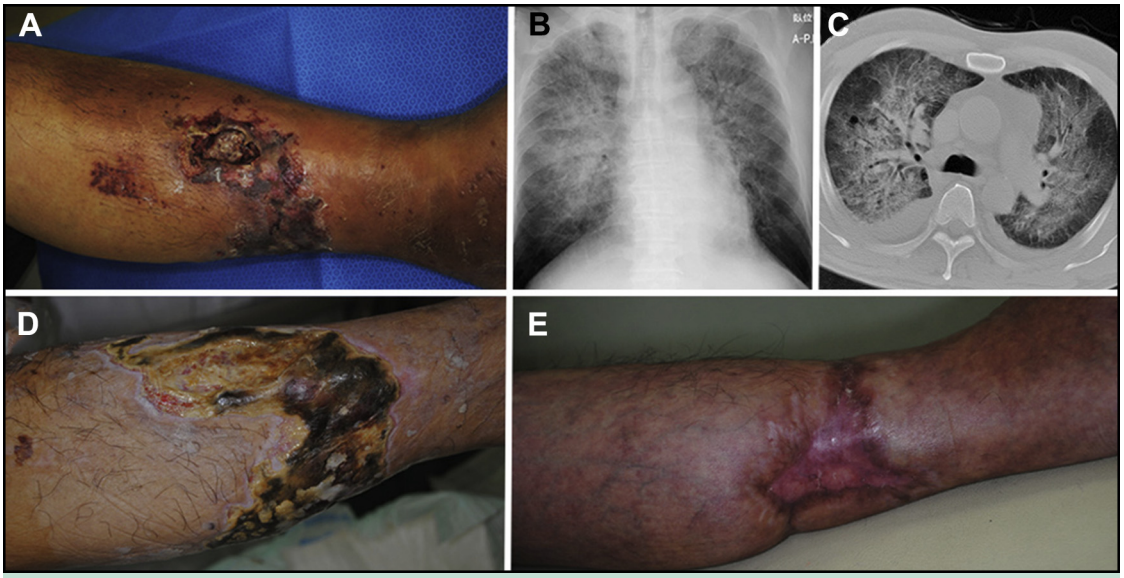

Figure Clinical manifestations of the left lower extremity, and X-ray and computed tomography images of the chest. (**A**) Painful deep ulcers with necrotic tissue and diffuse erosive purpura. (**B**) A butterfly shadow indicating pulmonary edema. (**C**) Ground-glass opacity and infiltrative shadows around bilateral hilar regions, thickening of interlobular septa, and bilateral pleural effusions are observed. (**D**) After methylprednisolone pulse treatment, the ulcers expanded with massive necrotic tissue. (**E**) After 11 months of treatment the ulcers have fully healed, with distinguishable scars reaching the muscles.

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5 days after admission. Chest X-ray and computed tomography images displayed butterfly appearance, ground-glass opacity, and infiltrative shadows in the hilar region, and bilateral pleural effusions (**Figures B** and **C**). Cardiac dysfunction was not observed. Blood gas demonstrated hypoxemia. Bacterial blood cultures were negative, and septic signs were not present. No other systemic diseases were detected. We made a diagnosis of pyoderma gangrenosum complicated with acute respiratory distress syndrome on the basis of these findings. Methylprednisolone pulse treatment was administered for 5 days. Enlargement of the ulcers persisted (**Figure D**). Oral prednisolone (initial dose: 1 mg/kg/d) was initiated and maintained for 4 weeks and was then gradually tapered. Respiratory symptoms largely disappeared within 4 weeks of treatment. The ulcers completely epithelized after an 11-month course of oral prednisolone (**Figure E**).

Systemic inflammatory diseases and trauma can incite pyoderma gangrenosum. The clinical course and symptoms of recurring ulcers without other specific histologic findings led us a pyoderma gangrenosum diagnosis. Acute respiratory distress syndrome is an acute-onset hypoxemia that occurs simultaneously with severe systemic conditions, such as sepsis and multiple trauma, and that presents a typical butterfly shadow in X-ray. It should be differentiated from cardiogenic pulmonary edema and frequently develops into multiple organ failure.[2] The pathomechanism of acute respiratory distress syndrome is considered to be lung injury caused by activated neutrophils, macrophages, and the cytokines they release.[3] Relatively little is known about the pathogenesis of pyoderma gangrenosum. Recently, several reports have noted that typical cytokines, including interleukin-6, interleukin-8, and granulocyte-colony stimulating factor, are elevated in pyoderma gangrenosum patients' serum.[1,4,5] These cytokines are thought to stimulate neutrophils. Because the acute respiratory distress syndrome in our case was accompanied by rapidly progressing cutaneous manifestations, cytokine storms produced by pyoderma gangrenosum may have contributed to the complication of acute respiratory distress syndrome. Systemic steroids were effective for pyoderma gangrenosum and acute respiratory distress syndrome. Our case highlights that aggressive disease activity in pyoderma gangrenosum can trigger acute respiratory distress syndrome and that efficacious diagnosis is essential.

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